

## CLAIMS

What is claimed is:

- 1 1. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the  
2 steps of:
  - 3 (a) providing a protein, a surfactant, and a lipid in a liquid carrier;
  - 4 (b) providing a crosslinker capable of crosslinking the protein;
  - 5 (c) preparing a sealant by mixing the protein with the crosslinker under  
6 conditions which permit crosslinking of the protein; and
  - 7 (d) applying the sealant of (c) to a tissue, thereby to bond the tissue or seal a  
8 fluid or gas leak in the tissue.
- 1 2. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the  
2 steps of:
  - 3 (a) applying to a tissue locus:
    - 4 i. a protein preparation;
    - 5 ii. at least one preparation selected from the group consisting of a  
6 surfactant preparation and a lipid preparation; and
    - 7 iii. a crosslinker preparation; and
  - 8 (b) permitting the preparations to form crosslinks, thereby to bond said tissue or  
9 to seal a fluid or gas leak in said tissue.
- 1 3. The method of claim 1 or 2, wherein the protein is selected from the group  
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.
- 1 4. The method of claim 3, wherein the concentration of the protein is between about  
2 3% (w/w) and about 50% (w/w).
- 1 5. The method of claim 4, wherein the protein is albumin and wherein the  
2 concentration of albumin is between about 20% (w/w) and about 50% (w/w).
- 1 6. The method of claim 4, wherein the protein is collagen and wherein the  
2 concentration of collagen is between about 3% (w/w) and about 12% (w/w).
- 1 7. The method of claim 4, wherein the protein is a globulin and wherein the  
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).

- 1 8. The method of claim 1 or 2, wherein the concentration of surfactant is between  
2 about 0.05% (w/w) and about 10% (w/w).
- 1 9. The method of claim 8, wherein the surfactant is an ionic surfactant.
- 1 10. The method of claim 9, wherein the ionic surfactant is selected from the group  
2 consisting of alkanoic acids, alkylsulfonic acids, alkyl amines, perfluoroalkanoic  
3 acids, and perfluoroalkylsulfonic acids.
- 1 11. The method of claim 10, wherein the ionic surfactant comprises an alkyl group  
2 with a chemical formula  $\text{CH}_3(\text{CH}_2)_n$ , wherein n is an integer from about 6 to  
3 about 18.
- 1 12. The method of claim 10, wherein the alkanoic acid is selected from the group  
2 consisting of octanoic acid, dodecanoic acid and palmitic acid.
- 1 13. The method of claim 10, wherein the alkylsulfonic acid is sodium lauryl sulfate.
- 1 14. The method of claim 10, wherein the perfluoroalkanoic acid has a structure  
2 selected from the group consisting of  $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$ , and  $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$ ,  
3 wherein n is an integer from one to about sixteen.
- 1 15. The method of claim 10, wherein the perfluoroalkanoic acid is perfluorooctanoic  
2 acid.
- 1 16. The method of claim 1 or 2, wherein the surfactant is a nonionic surfactant.
- 1 17. The method of claim 16, wherein the nonionic surfactant is selected from the  
2 group consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a  
3 polyoxyethylene ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether  
4 alcohol.
- 1 18. The method of claim 17, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 19. The method of claim 1 or 2, wherein the concentration of the lipid is from about  
2 0.1% (w/v) to about 10% (w/v).
- 1 20. The method of claim 1 or 2, wherein the lipid is a naturally-occurring lipid.
- 1 21. The method of claim 1 or 2, wherein the lipid is a synthetic lipid.

- 1 22. The method of claim 1 or 2, wherein the lipid is a hydrophobically-modified  
2 glycerol derivative of a molecule selected from the group consisting of  
3 phosphocholines, phosphatidic acid, phosphatidylethanolamine, phosphatidyl  
4 inositol, glycerol, bile acids, and long chain alcohols.
- 1 23. The method of claim 22, wherein the hydrophobically-modified glycerol derivative  
2 of a phosphocholine has the structure  $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$   
3  $OPO_2O(CH_2)_2-N(CH_3)_3$ , wherein  $R_1$  and  $R_2$  are chemical groups that do not react  
4 with a carbodiimide.
- 1 24. The method of claim 22, wherein the hydrophobically-modified glycerol derivative  
2 of a phosphatidic acid has the structure  $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$   
3  $OPO_2H$ , wherein  $R_1$  and  $R_2$  are chemical groups that do not react with a  
4 carbodiimide.
- 1 25. The method of claim 22, wherein the hydrophobically-modified glycerol derivative  
2 of a phosphatidylethanolamine has the structure  $R_1-C(O)-O-CH_2-(R_2-C(O)-$   
3  $O)CH_2-CH_2-OPO_2O(CH_2)_2-NH_2$ , wherein  $R_1$  and  $R_2$  are chemical groups that do  
4 not react with a carbodiimide.
- 1 26. The method of claim 22, wherein the hydrophobically modified glycerol derivative  
2 of a phosphatidyl inositol has the structure of  $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-$   
3  $CH_2-OPO_2O(C_6)_2H_{11}O_5$ , wherein  $R_1$  and  $R_2$  are chemical groups that do not  
4 react with a carbodiimide.
- 1 27. The method of claim 23-26, wherein the structure of  $R_1$  is  $CH_3(CH_2)_n-$ , wherein  
2 the structure of  $R_2$  is  $CH_3(CH_2)_m-$ , wherein  $n$  is an integer from about 4 to about  
3 22, and wherein  $m$  is an integer from about 4 to about 22.
- 1 28. The method of claim 23, wherein the hydrophobically-modified glycerol derivative  
2 of a phosphocholine is dipalmitoylphosphatidyl choline.
- 1 29. The method of claim 22, wherein the bile acid is selected from the group  
2 consisting of cholic acid, chenodeoxycholic acid, cholic acid methyl ester,  
3 dehydrocholic acid, deoxycholic acid, and lithocholic acid.
- 1 30. The method of claim 22, wherein the long chain alcohol has the structure  
2  $CH_3(CH_2)_n-OH$ , wherein  $n$  is an integer from about six to about twenty-two.

- 1 31. The method of claim 1 or 2, wherein the crosslinker is a zero-length, -  
2 homobifunctional, heterobifunctional, or multifunctional crosslinker.
- 1 32. The method of claim 31, wherein the zero-length crosslinker is selected from the  
2 group consisting of carbodiimides, isoxazolium salts, and carbonyldiimidazole
- 1 33. The method of claim 31, wherein the carbodiimide is 1-ethyl-3-(3-  
2 dimethylaminopropyl) carbodiimide hydrochloride (EDC)
- 1 34. The method of claim 32, wherein the concentration of EDC is from about 5 to  
2 about 500 mg/mL.
- 1 35. The method of claim 31, wherein the zerolength crosslinker is selected from the  
2 group consisting of a carbodiimide mediated reactive ester and a carbamate.
- 1 36. The method of claim 35, wherein the reactive ester is formed from N-  
2 hydroxysuccinimide or N-hydroxysulfosuccinimide.
- 1 37. The method of claim 1 or 2, wherein the surfactant is covalently attached to the  
2 protein.
- 1 38. The method of claim 1 or 2, wherein the surfactant is not covalently attached to  
2 the protein.
- 1 39. The method of claim 1 or 2, wherein the lipid is covalently attached to the protein.
- 1 40. The method of claim 1 or 2, wherein the lipid is not covalently attached to the  
2 protein.
- 1 41. A kit for producing a protein-based tissue adhesive or sealant comprising:  
2 (a) a protein preparation;  
3 (b) a protein-degrading preparation; and  
4 (c) a crosslinker preparation.
- 1 42. A kit for producing a protein-based tissue adhesive or sealant comprising:  
2 (a) a protein preparation;  
3 (b) a crosslinker preparation; and

- 4 (c) at least one preparation selected from the group consisting of a  
5 surfactant preparation and a lipid preparation.
- 1 43. The kit of claim 42 further comprising at least one preparation selected from the  
2 group consisting of a tissue primer preparation and a protein-degrading  
3 preparation.
- 1 44. The kit of claim 41 or 42, wherein the protein is selected from the group  
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.
- 1 45. The kit of claim 44, wherein the concentration of the protein is between about 3%  
2 (w/w) and about 50% (w/w).
- 1 46. The kit of claim 45, wherein the protein is albumin and wherein the concentration  
2 of albumin is between about 25% (w/w) and about 50% (w/w).
- 1 47. The kit of claim 45, wherein the protein is collagen and wherein the concentration  
2 of collagen is between about 3% (w/w) and about 12% (w/w).
- 1 48. The kit of claim 45, wherein the protein is a globulin and wherein the  
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).
- 1 49. The kit of claim 42, wherein the concentration of surfactant is between about  
2 0.05% (w/w) and about 10% (w/w).
- 1 50. The kit of claim 42, wherein the surfactant is an ionic surfactant.
- 1 51. The kit of claim 50, wherein the ionic surfactant is selected from the group  
2 consisting of alkanoic acids, alkylsulfonic acids, alkyl amines, perfluoroalkanoic  
3 acids, and perfluoroalkylsulfonic acids.
- 1 52. The kit of claim 50, wherein the ionic surfactant comprises an alkyl group with a  
2 chemical formula  $\text{CH}_3(\text{CH}_2)_n$ , wherein n is an integer from about 6 to about 18.
- 1 53. The kit of claim 51, wherein the alkanoic acid is selected from the group  
2 consisting of octanoic acid, dodecanoic acid and palmitic acid.
- 1 54. The kit of claim 51, wherein the alkylsulfonic acid is sodium lauryl sulfate.

- 1 55. The kit of claim 51, wherein the perfluoroalkanoic acid has a structure selected  
2 from the group consisting of  $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$ , and  $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$ , wherein  
3 n is an integer from one to about sixteen.
- 1 56. The kit of claim 51, wherein the perfluoroalkanoic acid is perfluorooctanoic acid.
- 1 57. The kit of claim 42, wherein the surfactant is a nonionic surfactant.
- 1 58. The kit of claim 57, wherein the nonionic surfactant is selected from the group  
2 consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a polyoxyethylene  
3 ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether alcohol.
- 1 59. The kit of claim 57, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 60. The kit of claim 42, wherein the concentration of the lipid is from about 0.1%  
2 (w/v) to about 10% (w/v).
- 1 61. The kit of claim 42, wherein the lipid is a naturally-occurring lipid.
- 1 62. The kit of claim 42, wherein the lipid is a synthetic lipid.
- 1 63. The kit of claim 42, wherein the lipid is a hydrophobically-modified glycerol  
2 derivative of a molecule selected from the group consisting of phosphocholines,  
3 phosphatidic acid, phosphatidylethanolamine, phosphatidyl inositol, glycerol, bile  
4 acids, and long chain alcohols.
- 1 64. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a  
2 phosphocholine has the structure  $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-CH}_2\text{-}$   
3  $\text{OPO}_2\text{O(CH}_2)_2\text{-N(CH}_3)_3$ , wherein  $\text{R}_1$  and  $\text{R}_2$  are chemical groups that do not react  
4 with a carbodiimide.
- 1 65. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a  
2 phosphatidic acid has the structure  $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-CH}_2\text{-}$   
3  $\text{OPO}_2\text{H}$ , wherein  $\text{R}_1$  and  $\text{R}_2$  are chemical groups that do not react with a  
4 carbodiimide.
- 1 66. The kit of claim 63, wherein the hydrophobically-modified glycerol derivative of a  
2 phosphatidylethanolamine has the structure  $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-O)CH}_2\text{-}$   
3  $\text{CH}_2\text{-OPO}_2\text{O(CH}_2)_2\text{-NH}_2$ , wherein  $\text{R}_1$  and  $\text{R}_2$  are chemical groups that do not  
4 react with a carbodiimide.

- 1 67. The kit of claim 63, wherein the hydrophobically modified glycerol derivative of a  
2 phosphatidyl inositol has the structure of  $R_1-C(O)-O-CH_2-(R_2-C(O)-O)CH_2-CH_2-$   
3  $OPO_2 O(C_6H_5)_2H_{11}O_5$ , wherein  $R_1$  and  $R_2$  are chemical groups that do not react  
4 with a carbodiimide.
- 1 68. The kit of claim 64-67, wherein the structure of  $R_1$  is  $CH_3(CH_2)_n-$ , wherein the  
2 structure of  $R_2$  is  $CH_3(CH_2)_m-$ , wherein  $n$  is an integer from about 4 to about 22,  
3 and wherein  $m$  is an integer from about 4 to about 22.
- 1 69. The kit of claim 64, wherein the hydrophobically-modified glycerol derivative of a  
2 phosphocholine is dipalmitoylphosphatidyl choline.
- 1 70. The kit of claim 63, wherein the bile acid is selected from the group consisting of  
2 cholic acid, chenodeoxycholic acid, cholic acid methyl ester, dehydrocholic acid,  
3 deoxycholic acid, and lithocholic acid.
- 1 71. The kit of claim 63, wherein the long chain alcohol has the structure  $CH_3(CH_2)_n-$   
2  $OH$ , wherein  $n$  is an integer from about six to about twenty-two.
- 1 72. The kit of claim 41 or 42, wherein the crosslinker is a zero-length,  
2 homobifunctional, heterobifunctional, or multifunctional crosslinker.
- 1 73. The kit of claim 72, wherein the zero-length crosslinker is selected from the  
2 group consisting of carbodiimides, isoxazolium salts, and carbonyldiimidazole.
- 1 74. The kit of claim 73, wherein the carbodiimide is 1-ethyl-3-(3-  
2 dimethylaminopropyl) carbodiimide hydrochloride (EDC).
- 1 75. The kit of claim 74, wherein the concentration of EDC is from about 5 to about  
2 500 mg/mL.
- 1 76. The kit of claim 72, wherein the zero-length crosslinker is selected from the  
2 group consisting of a carbodiimide mediated reactive ester and a carbamate.
- 1 77. The kit of claim 76, wherein the reactive ester is formed from N-  
2 hydroxysuccinimide or N-hydroxysulfosuccinimide.
- 1 78. The kit of claim 42, wherein the surfactant is covalently attached to the protein.

- 1 79. The kit of claim 42, wherein the surfactant is not covalently attached to the  
2 protein.
- 1 80. The kit of claim 42, wherein the lipid is covalently attached to the protein.
- 1 81. The kit of claim 42, wherein the lipid is not covalently attached to the protein.
- 1 82. A platelet-free composition for use as a tissue sealant or adhesive comprising a  
2 protein solution and at least one preparation selected from the group consisting  
3 of a surfactant preparation and a lipid preparation.
- 1 83. The composition of claim 82 comprising a protein solution, a surfactant  
2 preparation and a lipid preparation.
- 1 84. The composition of claim 82, wherein the protein is selected from the group  
2 consisting of albumin, collagen, gelatin, globulin, elastin, protamine, and histone.
- 1 85. The composition of claim 84, wherein the concentration of the protein is between  
2 about 3% (w/w) and 50% (w/w).
- 1 86. The composition of claim 85, wherein the protein is albumin and wherein the  
2 concentration of albumin is between about 25% (w/w) and about 50% (w/w)
- 1 87. The composition of claim 85, wherein the protein is collagen and wherein the  
2 concentration of collagen is between about 3% (w/w) and about 12% (w/w).
- 1 88. The composition of claim 85, wherein the protein is a globulin and wherein the  
2 concentration of the globulin is between about 15% (w/w) and about 30% (w/w).
- 1 89. The composition of claim 82, wherein the concentration of surfactant is between  
2 about 0.05% (w/w) and about 10% (w/w).
- 1 90. The composition of claim 82, wherein the surfactant is an ionic surfactant.
- 1 91. The composition of claim 90, wherein the ionic surfactant is selected from the  
2 group consisting of alkanoic acids, alkylsulfonic acids, alkyl amines,  
3 perfluoroalkanoic acids, and perfluoroalkylsulfonic acids.
- 1 92. The composition of claim 91, wherein the ionic surfactant comprises an alkyl  
2 group with a chemical formula  $\text{CH}_3(\text{CH}_2)_n$ , wherein n is an integer from about 6  
3 to about 18.



- 1 93. The composition of claim 91, wherein the alkanoic acid is selected from the  
2 group consisting of octanoic acid, dodecanoic acid and palmitic acid.
- 1 94. The composition of claim 91, wherein the alkylsulfonic acid is sodium lauryl  
2 sulfate.
- 1 95. The composition of claim 91, wherein the perfluoroalkanoic acid has a structure  
2 selected from the group consisting of  $\text{CF}_3(\text{CF}_2)_n\text{-COO-}$ , and  $\text{-OOC}(\text{CF}_2)_n\text{-COO-}$ ,  
3 wherein n is an integer from one to about sixteen.
- 1 96. The composition of claim 91, wherein the perfluoroalkanoic acid is  
2 perfluorooctanoic acid.
- 1 97. The composition of claim 82, wherein the surfactant is a nonionic surfactant.
- 1 98. The composition of claim 97, wherein the nonionic surfactant is selected from the  
2 group consisting of an alkyl or perfluoroalkyl- polyoxyethylene ether, a  
3 polyoxyethylene ester, a polyoxyethylene sorbitan, and an alkyl aryl polyether  
4 alcohol.
- 1 99. The composition of claim 98, wherein the alkyl aryl polyether alcohol is tyloxapol.
- 1 100. The composition of claim 82, wherein the concentration of the lipid is from about  
2 0.1% (w/v) to about 10% (w/v).
- 1 101. The composition of claim 82, wherein the lipid is a naturally-occurring lipid.
- 1 102. The composition of claim 82, wherein the lipid is a synthetic lipid.
- 1 103. The composition of claim 82, wherein the lipid is a hydrophobically-modified  
2 glycerol derivative of a molecule selected from the group consisting of  
3 phosphocholines, phosphatidic acid, phosphatidylethanolamine, phosphatidyl  
4 inositol, glycerol, bile acids, and long chain alcohols.
- 1 104. The composition of claim 103, wherein the hydrophobically-modified glycerol  
2 derivative of a phosphocholine has the structure  $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-}$   
3  $\text{O)CH}_2\text{-CH}_2\text{-OPO}_2\text{O(CH}_2)_2\text{-N(CH}_3)_3$ , wherein  $\text{R}_1$  and  $\text{R}_2$  are chemical groups that  
4 do not react with a carbodiimide.
- 1 105. The composition of claim 103, wherein the hydrophobically-modified glycerol  
2 derivativ of a phosphatidic acid has the structur  $\text{R}_1\text{-C(O)-O-CH}_2\text{-(R}_2\text{-C(O)-}$

3 O)CH<sub>2</sub>-CH<sub>2</sub>-OPO<sub>2</sub>H, wherein R<sub>1</sub> and R<sub>2</sub> are chemical groups that do not react  
4 with a carbodiimide.

1 106. The composition of claim 103, wherein the hydrophobically-modified glycerol  
2 derivative of a phosphatidylethanolamine has the structure R<sub>1</sub>-C(O)-O-CH<sub>2</sub>-(R<sub>2</sub>-  
3 C(O)-O)CH<sub>2</sub>-CH<sub>2</sub>-OPO<sub>2</sub> O(CH<sub>2</sub>)<sub>2</sub>-NH<sub>2</sub>, wherein R<sub>1</sub> and R<sub>2</sub> are chemical groups  
4 that do not react with a carbodiimide.

1 107. The composition of claim 103, wherein the hydrophobically modified glycerol  
2 derivative of a phosphatidyl inositol has the structure of R<sub>1</sub>-C(O)-O-CH<sub>2</sub>-(R<sub>2</sub>-  
3 C(O)-O)CH<sub>2</sub>-CH<sub>2</sub>-OPO<sub>2</sub> O(C<sub>6</sub>)<sub>2</sub>H<sub>11</sub>O<sub>5</sub>, wherein R<sub>1</sub> and R<sub>2</sub> are chemical groups  
4 that do not react with a carbodiimide.

1 108. The composition of claim 104-107, wherein the structure of R<sub>1</sub> is CH<sub>3</sub>(CH<sub>2</sub>)<sub>n</sub>-,  
2 wherein the structure of R<sub>2</sub> is CH<sub>3</sub>(CH<sub>2</sub>)<sub>m</sub>-, wherein n is an integer from about 4  
3 to about 22, and wherein m is an integer from about 4 to about 22.

1 109. The composition of claim 104, wherein the hydrophobically-modified glycerol  
2 derivative of a phosphocholine is dipalmitoylphosphatidyl choline.

1 110. The composition of claim 103, wherein the bile acid is selected from the group  
2 consisting of cholic acid, chenodeoxycholic acid, cholic acid methyl ester,  
3 dehydrocholic acid, deoxycholic acid, and lithocholic acid.

1 111. The composition of claim 103, wherein the long chain alcohol has the structure  
2 CH<sub>3</sub>(CH<sub>2</sub>)<sub>n</sub>-OH, wherein n is an integer from about six to about twenty-two.

1 112. The composition of claim 82, wherein the surfactant is covalently attached to the  
2 protein.

1 113. The composition of claim 82, wherein the surfactant is not covalently attached to  
2 the protein.

1 114. The composition of claim 82, wherein the lipid is covalently attached to the  
2 protein.

1 115. The composition of claim 82, wherein the lipid is not covalently attached to the  
2 protein.

- 1 116. A method for preparing a tissue to react with a protein-based tissue sealant or  
2 adhesive comprising the step of:  
3           applying a primer solution at a pH of about 3.0 to 9.0 to a tissue locus.
- 1 117. The method of claim 116, wherein the primer solution comprises a buffer.
- 1 118. The method of claim 117, wherein the buffer is morpholinoethanesulfonic acid.
- 1 119. The method of claim 118, wherein the pH is about 5.
- 1 120. The method of claim 118, wherein the concentration of the buffer is about 0.5M.
- 1 121. A method for preparing a tissue to react with a protein-based tissue sealant or  
2 adhesive comprising the step of:  
1           applying a primer solution containing a protein crosslinker to a tissue  
2 locus.
- 1 122. The method of claim 121, wherein the crosslinker is carbodiimide.
- 1 123. The method of claim 122, wherein the carbodiimide is EDC-HCl.
- 1 124. The method of claim 121, wherein the primer is a solution of carbodiimide and  
2 hydroxysuccinimide.
- 1 125. The method of claim 124, wherein the carbodiimide is EDC-HCl and the  
2 hydroxysuccinimide is N-hydroxysulfosuccinimide.
- 1 126. The method of claim 121, wherein the primer is a solution of a dialdehyde or a  
2 polyaldehyde.
- 1 127. The method of claim 126, wherein the primer comprises glutaraldehyde or a  
2 derivative thereof.
- 1 128. A method for preparing a tissue to react with a protein-based tissue sealant or  
2 adhesive comprising the step of:  
3           applying a primer solution comprising a molecule that promotes contact  
4 between the sealant and a tissue, thereby promoting an increase in reactive  
5 surface area between the sealant and the tissue.
- 1 129. The method of claim 128, wherein the molecule interacts preferentially with  
2 fluorophilic surfaces.

- 1 130. The method of claim 128, wherein the molecule comprises a fluorophilic moiety.
- 1 131. The method of claim 130, wherein the fluorophilic moiety is a perfluoroalkanoic  
2 acid.
- 1 132. The method of claim 131, wherein the perfluoroalkanoic acid is perfluorooctanoic  
2 acid.
- 1 133. A method for increasing the degradation rate, or reducing the persistence of a  
2 polymer-based tissue sealant or adhesive, comprising the step of:  
3 mixing a polymer degrading agent with a sealant or adhesive before  
4 applying the sealant or adhesive to a tissue.
- 1 134. A method for increasing the degradation rate, or reducing the persistence of a  
2 polymer-based tissue sealant or adhesive, comprising the step of:  
3 applying a polymer degrading agent to a sealant or adhesive at a tissue  
4 locus, thereby increasing the degradation rate of the sealant or adhesive at the  
5 tissue.
- 1 135. The method of claim 133 or 134, wherein the sealant or adhesive is selected  
2 from the group consisting of protein-based, carbohydrate-based, nucleotide-  
3 based, and synthetic polymer-based tissue sealants or adhesives or any  
4 combination thereof.
- 1 136. The method of claim 133, wherein said tissue sealant or adhesive is protein-  
2 based.
- 1 137. The method of claim 136, wherein the protein is selected from the group  
2 consisting of albumin, collagen, and globulin.
- 1 138. The method of claim 133 or 134, wherein the sealant or adhesive is  
2 carbohydrate-based.
- 1 139. The method of claim 138, wherein the carbohydrate is selected from the group  
2 consisting of natural and synthetic poly- and oligo-saccharides.
- 1 140. The method of claim 139, wherein the carbohydrate is selected from the group  
2 consisting of amylose, amylopectin, alginate, agarose, cellulose,

- 3 carboxymethylcellulose, carboxymethylamylose, chitin, chitosan, pectin, and  
4 dextran.
- 1 141. The method of claim 133 or 134, wherein the degradation agent is an enzyme.
- 1 142. The method of claim 141, wherein the enzyme is selected from the group  
2 consisting of proteases and glucanases.
- 1 143. The method of claim 142, wherein the protease is selected from the group  
2 consisting of bromelain, trypsin, chymotrypsin, clostripain, collagenase, elastase,  
3 papain, proteinase K, pepsin, and subtilisin.
- 1 144. The method of claim 143, wherein the protease is trypsin.
- 1 145. The method of claim 142, wherein the glucanase is selected from the group  
2 consisting of agarases, amylases, cellulases, chitinases, dextranases,  
3 hyaluranidases, lysozymes, and pectinases.
- 1 146. The method of claim 145, wherein the glucanase is cellulase.
- 1 147. The method of claim 133 or 134, wherein the degradation agent is provided in an  
2 amount sufficient to promote degradation of the tissue sealant or adhesive within  
3 forty days.
- 1 148. The method of claim 133 or 134, wherein the degradation agent is provided in an  
2 inactive form, and wherein the degradation agent is activated after its application  
3 to the sealant or adhesive.
- 1 149. The method of claim 133 or 134, wherein the tissue is selected from the group  
2 consisting of connective tissue, vascular tissue, pulmonary tissue, neural tissue,  
3 lymphatic tissue, dural tissue, spleen tissue, hepatic tissue, renal tissue,  
4 gastrointestinal tissue, and skin.
- 1 150. A method for bonding tissue or sealing a fluid or gas leak in tissue comprising the  
2 steps of:  
3 (a) providing a solution comprising about 35% BSA, 5% DPPC, and 5%  
4 Tyloxapol;  
5 (b) providing a solution of about 200 mg/ml EDC;

- 6 (c) preparing a sealant by mixing the solution of step (a) with the solution of  
7 step (b) in a ratio of about 10/1 (v/v); and  
8 (d) applying the sealant of step (c) to a tissue, thereby to bond the tissue or  
9 seal a fluid or gas leak in the tissue.

1 151. A kit for producing a protein-based tissue adhesive or sealant comprising:

- 2 (a) a solution comprising about 35% BSA;  
3 (b) a crosslinker preparation comprising about 20% EDC; and  
4 (c) at least one preparation selected from the group consisting of about  
5 5% DPPC, about 5% Tyloxapol, and a combination thereof.

1 152. A two- component kit for producing a protein-based tissue adhesive or sealant  
2 comprising:

- 3 (a) a first protein preparation; and,  
4 (b) a second protein preparation mixed with a cross-linker preparation.

1 153. The kit of claim 152, wherein said first protein preparation is at an acid pH and  
2 said second protein preparation is at a basic pH.

1 154. A two-component kit for producing a tissue adhesive or sealant comprising:

- 2 (a) a first sealant component at an acid pH;  
3 (b) a second sealant component at a basic pH; and,  
4 (c) a cross-linker preparation that is active at an intermediate pH,  
5 wherein the cross-linker is activated upon mixing of (a), (b), and (c).

1 155. The kit of claim 153, wherein the pH of said first protein preparation is between  
2 about 3.0 and 6.0.

1 156. The kit of claim 153, wherein the pH of said second protein preparation is  
2 between about 6.5 and 10.0.

1 157. The kit of claim 152, wherein said first protein preparation and said second  
2 protein preparation are selected from the group consisting of albumin, collagen,  
3 gelatin, globulins, protamine, and histones.

1 158. The kit of claim 157, wherein said first protein preparation and said second  
2 protein preparation comprise between about 3% (w/w) and about 50%(w/w) of  
3 protein.

1 159. The kit of claim 157, wherein said first protein preparation and said second  
2 protein preparation comprise albumin at between about 15% (w/w) and about  
3 50%(w/w).

1 160. A kit for producing a protein-based tissue adhesive or sealant comprising:  
2 (a) a preparation comprising a protein and a carbohydrate;  
3 (b) a degradation agent; and,  
4 (c) a cross-linker preparation.

1 161. The kit of claim 160, wherein said protein is selected from the the group  
2 consisting of albumin, collagen, gelatin, globulins, protamine, and histones.

1 162. The kit of claim 160, wherein said protein is at a concentration of between about  
2 15% and about 40%.

1 163. The kit of claim 160, wherein said carbohydrate is selected from the group  
2 consisting of natural and synthetic poly- and oligo-saccharides.

1 164. The kit of claim 160, wherein said carbohydrate is selected from the group  
2 consisting of of amylose, amylopectin, alginate, agarose, cellulose,  
3 carboxymethylcellulose, carboxymethylamylose, chitin, chitosan, pectin, and  
4 dextran.

1 165. The kit of claim 160, wherein said carbohydrate is at a concentration of between  
2 about about 0.1% (w/w) and about 10% (w/w).

1 166. The kit of claim 160, wherein said degradation agent is selected from the group  
2 consisting of proteases and glucanases.

1 167. The kit of claim 166, wherein said glucanases is an alginase.